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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/512,096	12/27/2005	Akira Yagi	2520-0131PUS1	8923

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BIRCH STEWART KOLASCH & BIRCH
PO BOX 747
FALLS CHURCH, VA 22040-0747

EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
02/11/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

mailroom@bskb.com

Office Action Summary	Application No.	Applicant(s)	
	10/512,096	YAGI ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *7-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Applicant's remarks and amendments to the claims dated 11/2/07 is acknowledged.

Status of Claims

Claims 7-12 are pending in the application.

Claims 1-6 were cancelled.

Status of Office Action: Final.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 7-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yagi et al. EP1067138 (hereinafter Yagi) in view of Iwasaki et al. Study of liver function

in babies with atopic dermatitis by using 13-C-methacetin breath test, Arerugi, 1992 Jun;41(6):645-53 (hereinafter Iwasaki) and further in view of Kimata H. Fatty Liver in Atopic dermatitis, Allergy. 2001 May;56(5):460 (hereinafter Kimata).

Yagi teaches hydroxyproline derivative such as the structure of Compound 2 disclosed, which is 3'-Hydroxymethyl-4-hydroxypyrrolido [1,2-f] 2', 5'-piperazinedione, (see formula 3-1). The composition can be topically administered in the form of powders, granules, and ointments, and being administered orally or non-orally [0022].

Yagi teaches the use of hydroxyproline derivative such as 3'-Hydroxymethyl-4-hydroxypyrrolido [1,2-f] 2', 5'-piperazinedione for the treatment of liver damage and discloses that the efficacy which is expected for the compounds of the invention is illustrated as follows:

(1) Decrease in activities of cytosolic enzymes (GOT, GPT, gamma -GTP, ALP, LAP and LDH, etc.) in a damaged liver.

(2) Increase in the hepatic uptake of bilirubin.

(3) Hepatoprotection (prevention and suppression of degeneration and necrosis of hepatocytes).

(4) Suppression of hepatofibrosis and hyperplasia of hepatic fibrous tissue, and absorption of hyperplastic hepatic fibrous tissue and interstitial connective tissues.

(5) Anti-hepatolipocytosis (decrease in lipid precipitation to a liver and improvement of lipid degeneration in hepatocytes).

(6) Activation of tissue respiration (Activation of succinic acid dehydrogenase and

stimulation of tissue respiration in a liver, and activation of metabolism in hepatocytes) (7) Stabilization of hepatocyte membrane.

Yagi does not teach explicitly the treatment of allergies by the compound disclosed.

Iwasaki teaches the relation between liver damage and atopic dermatitis. The reference discloses that level of serum Got levels is higher in babies with atopic dermatitis and food allergies.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the compound disclosed by Yagi in the form of topical administration to treat atopic dermatitis because Iwasak i teaches the relation between the liver serum GOT elevation (disclosed by Yagi to be corrected by the compound disclosed) and atopic dermatitis.

Iwasaki does not teach relation between liver damage and other types of allergy.

Kimata teaches the relation between fatty liver and other types of allergy such as allergic rhinitis and also atopic dermatitis. Kimata teaches that in cases of fatty liver (type of liver damage as disclosed by Yagi) there are tendency in the patients to have atopic dermatitis, and allergic rhinitis (see table 1).

It would have been obvious one of ordinary skill in the art at the time the invention was made to use the compound disclosed by Yagi in the form of topical administration to treat allergic rhinitis and atopic dermatitis because Kimata teaches that it has been reported that liver dysfunction is sometimes found in children with these types of allergies. Accordingly, it would have been obvious that treating liver problems taught by

Yagi would improve allergies. The expected results would be a topical administration of a composition comprising 3'-Hydroxymethyl-4-hydroxypyrrolido [1,2-f] 2', 5'-piperazinedione to treat allergies such as atopic dermatitis and allergic rhinitis.

Accordingly, it is inherent that these compounds would be effective in treating allergies such as rhinitis, and atopic dermatitis as recited in the instant claims.

Response to Arguments

4. Applicant's arguments filed 11/2/07 have been fully considered but they are not persuasive. Applicant argues that:

- The references (Iwasaki and Kimata) only disclose the relation between liver disease and allergy disease, and the references do not disclose that the liver disease causes the allergy disease. Further, these references do not teach that the atopic disease is improved by the treatment of liver disease. On the contrary, it is also possible that the liver disease is caused by the allergy disease.

To respond: The relation between liver disease and atopic diseases is enough to establish a prima facie case of obviousness. If the relation is established, then both problems may have a common etiology, or one may cause the other. However, when a compound is known to treat one of the two related. A person of ordinary skill in the art has a finite number of options to try because it would have been obvious to try the instant compound that treats liver conditions on other problems related with liver conditions since a person of ordinary skill has good reason to pursue the known options within his technical grasp. If this leads to improving the allergies related to liver

conditions, it is likely the product not of innovation but of ordinary skill and common sense.

- Iwasaki describes that there is some relationship between atopic dermatitis and liver dysfunction, since the serum GOT levers of atopic dermatitis patients are higher than normal. On the other hand, Kimata describes "the severity of fatty liver was not associated with liver dysfunction in that the serum levels of GOT and GPT were within normal limits in most of the patients with fatty liver" (the last paragraph of middle column). The contents of Iwasaki and Kimata are thus contradictory.

To respond: Kimata discloses that the severity of fatty liver in the group of patients tested was not associated with liver dysfunction in that the serum levels of GOT and GPT were within normal limits in most of the patients with fatty liver. Note that the patients were categorized as mild and moderate and not severe cases were recognized in that group of cases. Accordingly, it was expected that mild cases would mostly have serum levels of GOT and GPT within normal or at the borderline. (see last paragraph in the middle column).

- According to the percentage of 17.6% of atopic dermatitis patients. fatty liver is not thought to be a main factor in the cause of atopic dermatitis.

To respond: the relation between the two condition does not relate to which leads to the other, however, it gives obviousness to a person of ordinary skill in the art to try the treatment of liver conditions to atopic dermatitis. For example pain and fever are related conditions related to inflammation and both are improved by aspirin.

- According to the Examiner's view, all medicines used for the treatment of liver diseases will be effective in the treatment of an allergy disease.

To respond: This was not found persuasive because it would have been obvious to try the instant compound that treats liver conditions on other problems related with liver conditions because a person of ordinary skill has good reason to pursue the known options within his technical grasp. If this leads to improving the allergies related to liver conditions, it is likely the product not of innovation but of ordinary skill and common sense.

Conclusion

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim
4/13/07

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER